UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/530,907	06/30/2000	RUDI WILFRIED JAN PAUWELS	07619.0006	4853

45511 7590 07/20/2006

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE
46TH FLOOR
PHILADELPHIA, PA 19103

EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/530,907	PAUWELS ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/26/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,10,17,18,24,26,29,30 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,10,17,18,24,26,29,30 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 5, 10, 17, 18, 24, 26, 29, 30, and 32-35 are pending and examined.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/26/2006, has been entered.

3. Applicant in the new arguments, entered 4/26/2006, at p. 5 of 8, first paragraph, states: "Applicants are not amending the claims or specification."

Priority

4. The instant application, with a 371(c) date of 6/30/2000, is the national stage of PCT/IB98/01399, filed 9/8/1999.

Maintained Claim Rejections - 35 USC § 102

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 5, 10, 17, 18, 24, 26, 29, 30, and 32-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Bjornson et al., (US 6,284,113 B1, priority to 19 September 1997, of record). This rejection is maintained for the reasons of record, as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to methods for screening for analytes comprising the steps of a) disposing a plurality of analytes to be screened within individually identifiable containers such that the analytes remain isolated from each other, wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array: b) dispensing the analytes through the open ends of the capillary tubes onto at least one solid support to maintain the transferred contents of each container separate from those of each other container, wherein said analytes are simultaneously applied onto the at least one solid support; (c) contacting said at least one analyte-carrying solid support with targets provided in a semi-solid or liquid medium, whereby said analytes are released from the at least one solid support to the targets, wherein each analyte when applied to the solid support diffuses thereon so as to produce a concentration gradient; and (d) measuring analyte-target interactions, wherein said analyte-target interactions are measured using one or more of the following methods: microscopic, luminometric, densitometric, isotopic, and physical measurements; and variations thereof.

Bjornson et al., throughout the patent and abstract, teach methods wherein analytes or beads may be disposed within individually identifiable containers within microarray plates, and transferring the analytes or beads from the containers to microarray substrates in such a manner as to maintain the transferred contents of each container separate from those of each other container in the other microarray; wherein the microarrays comprise individually identifiable containers are in an array (e.g., col. 19, line 13; col. 20, line 13, Fig.s 6-8) of capillary tubes, including capillary tubes, and channels of capillary dimensions (col. 8, line 64-col. 9, line 4; col. 11, lines 6-10; col. 15, line 40-col. 16, line 67); wherein the microarray plates comprise individually identifiable cavity structures, reading on containers, and arrays of capillary channels, reading on capillary tubes, each of which is identifiable according to its position within the microfluidic network plate, and further comprising a array of microfluidic networks, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through apertures that are the open ends of the capillary channels (e.g., Fig. 4A, col. 16, lines 18-54); at col., e.g., col. 20, lines 46-53, teach microarray plates reading upon a solid support, wherein the microarray plates are information carriers which carry information in electronic and digitized form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a microarray plate that is a multi-compartmented apparatus; wherein said compartments are an arrangement of mini-wells in said apparatus; and at col. 9, lines 23-55, teach electroflow media,

reading on solvents, wherein said media includes polysaccharides, agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels.

Diffusion of analytes when applied to a solid support that is provided a gel, such as an agarose gel or a polymers hydrogel, whereupon a concentration gradient is formed, would be an inherent physical phenomenon, as evidenced by the publication of Gray et al., US 2005/0106380 A1. Gray et al. state:

> Generally, diffusion may be either active and/or passive. In passive diffusion the molecule simply passes through a porous polymer opening in response to a concentration gradient and does not interact with the polymer. The passive diffusion rate is a function of polymer molecular size. For example, oxygen diffuses at a faster rate through LDPE than through HDPE. Passive diffusion is also a function of pore size and concentration gradient, and high exchange rates can occur with large pore size. Diffusion rate is also a function of the size of the diffusing molecule. For instance, for a given polymer, the diffusion rate for the following molecules is listed in the order of highest to lowest: oxygen, water, methanol and ethanol. Passive diffusion can be affected by factors such as polymer crosslinking and polymer elongation through stretching, vacuum packing or shrink wrapping. Generally passive permeability decreases with increasing degrees of crosslinking and elongation.

Gray et al., at p. 4, para [0031]. Thus, upon delivery of analytes to porous polymers, such as those taught by Bjornson et al., at col.s 9-10, passive diffusion of the analyte would inherently produce a concentration gradient, as in claim 1.

Bjornson et al., at col. 18, lines 24-61, especially lines 56-59; col. 30, line 56-col. 31, line 14, disclose the manipulation of bead and particles in the channels of their disclosed microfluidic arrays. Bjornson et al. at col. 29, line 66-col. 30, line 14, teach using microfluidic processing for assays to determine specific binding pair members, as in determining an analyte, and include cell surface binding assays, assays for drug discovery and screening, and studies of receptors. Bjornson at, e.g., col. 28, lines 37-42, teach methods that employ detection means including, but not limited to spectrophotometric, chemiluminescent, electrochemical or radio chemical means. Bjornson at, e.g., col. 20, lines 46-65, teach the use of an electronic computer connected to electrodes, wherein the electrodes are interactive with an optical detection device such as ultraviolet or fluorescent spectrometer. Bjornson at, e.g., col. 24, lines 27-43, disclose dispensing liquid drops through capillary size dispensing tubes onto substrates surfaces in miniature arrays, where the printed arrays may consist of nucleic acids, peptides, immunoassay reagents, pharmaceutical test compounds and the like.

Response to Arguments

Applicant argues that the reference of Bjornson et al. does not teach all of the limitations of the claimed invention. Applicant argues that Bjornson et al. do not teach the measuring of analyte-target interactions as required in step (d). Applicant argues that while Bjornson et al., at col. 28, lines 37-42, describe "generally how label or reporter molecules can be used in assays and screening methods, and detected via spectrophotometric, chemiluminescent, electrochemical, or radiochemical means", Bjornson et al. do not disclose measuring analyte-target interactions, as claimed.

Applicant's arguments, entered 4/26/2006, have been fully considered but they are not persuasive. Bjornson et al., at col. 1, lines 8-18, teach their invention as useful for the generation of combinatorial libraries and high throughput screening in, for example, pharmaceutical drug discovery and genomic science applications. For example, at col. 1, lines 56-60, teach that receptors and enzymes may be targets in primary screens in order to identify agonist or antagonists. Bjornson et al., at col. 2, lines 9-24, consider combinatorial libraries that provide compounds for testing using binding assays. These binding assays characterize receptor-ligand interactions. The examiner respectfully submits that receptor-ligand interactions read upon the "analyte-target interactions" of the claimed invention.

The instant specification at p. 10, line 6-9, states that "[t]he analytes for rapid screening in the method according to the invention are preferably selected from chemical compounds, antigens, antibodies, DNA-probes, cell and beads and liposome carrying an analyte of interest."

Bjornson et al., at col. 28, lines 23-36, teach that a ligand can be any organic compound for which a receptor naturally exists or can be prepared. Bjornson et al., at col. col. 28, lines 24-27, state: "Receptors ("antiligand") are any compound or composition capable of recognizing a particular spatial and polar organizations of a molecule, e.g., epitopic or determinant site." Bjornson et al., in the citation referred to by applicant, teach that label or reporter molecules are for detection by a suitable detection means. Bjornson at col. 28, lines 53-55, states that "[r]eporter molecules are members of a signal producing system capable of being detected directly or through a

specific binding reaction to produce a detectable signal." Bjornson et al., at col. 20, lines 34-55, teach that assays comprise signals from labels that may be measured. Therefore, Bjornson et al. teach that measurement, or quantification, is an established aspect of a receptor-ligand assay. Therefore, the examiner respectfully submits that Bjornson et al. anticipate the claimed invention.

Maintained Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1-7, 9, 10, 17-19, 24, and 26-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al., US 5,601,992, (of record) and Bjornson et al., (US 6,284,113 B1, priority to 19 September 1997, of record). This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to methods for screening of analytes, comprising the steps of: a) simultaneously applying a plurality of analytes to be screened onto at least one solid support such that the analytes remain isolated from one another; b) contacting said at least one analyte-carrying solid support with targets provided in a semi-solid or liquid medium, whereby said analytes are released from the at least one solid support to the targets; and c) measuring analyte-target interactions.

The claims are further drawn to methods according to Claim 1, wherein step (a) comprises (i) disposing the analytes within individually identifiable containers, and (ii) transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, including capillary tubes, pens, including plotter pens, and print heads, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic, magnetic or digitised form, (as in claim 18); wherein each analyte-bearing solid

support is contacted in step b) with a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes gelatin, polysaccharides such as agar and agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels, gels containing N-isopropylacrylamide, or thermo-sensitive polymers, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31). The claimed invention is interpreted in view of the rejection under 35 USC 112, Second Paragraph (discussed above in the instant Office action).

Lerner et al., discloses a method that reads on that of the instant claims. Specifically, the reference discloses detecting the interaction between an oligomeric molecule (reading on claimed analyte) and a target (see, e.g. Abstract). In the method of Lerner et al, a plurality of beads containing peptide analytes are applied to a substrate surface and allowed to diffuse therein (see, e.g. column 21, lines 33-66 – "[t]he oligomeric molecules diffuse through the substrate and interact with a target"). This reads on the claimed step b) of releasing the analytes from the solid supports. The reference also reads on step a) of having analytes on at least one solid support in an isolated fashion, see, for example, column 3, lines 5-22). Beads as solid supports are used for the peptide analytes and the interaction tests were run in culture dishes (see, e.g. Examples 1 & 3 of the reference), this reads on the supports recited in the instant claims. The culture dishes of the reference have gels thereon, see, for example, column 29, lines 62-66. This reads on a coated solid support as recited in the instant claims. The peptide analytes and their preparations (see, e.g. Example 1) read on the analytes recited in instant claims 29, 30 and 32. Various cellular targets are also described by the reference (see Example 2 and column 21, line 66 - column 22, line 67) reading on claim 33. In the reference, pigment dispersion is measured (see, e.g. column 25, line 55 - column 26, line 52); this reads on the limitations of instant claim 36.

Lerner et al. does not teach methods according to Claim 1, wherein step (a) comprises (i) disposing the analytes within individually identifiable containers, and (ii) transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, including capillary tubes, pens, including plotter pens, and print heads, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic, magnetic or digitised form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes gelatin, polysaccharides such as agar and agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels, gels containing N-isopropylacrylamide, or thermo-sensitive polymers, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31).

Bjornson et al., throughout the patent and abstract, teach methods wherein analytes or beads may be disposed within individually identifiable containers within microarray plates, and transferring the analytes or beads from the containers to microarray substrates in such a manner as to maintain the transferred contents of each container separate from those of each other container in the other microarray, (as in claim 2); wherein the microarrays comprise individually identifiable containers are in an array (e.g., col. 19, line 13; col. 20, line 13, Fig.s 6-8) of capillary tubes, including capillary tubes, and channels of capillary dimensions (col. 8, line 64-col. 9, line 4; col. 11, lines 6-10; col. 15, line 40-col. 16, line 67), (as in claim 3); wherein the microarray plates comprise individually identifiable cavity structures, reading on containers, and arrays of capillary channels, reading on capillary tubes, each of which is identifiable according to its position within the microfluidic network plate, and further comprising a array of microfluidic networks, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through apertures that are the open ends of the capillary channels (e.g., Fig. 4A, col. 16, lines 18-54), (as in claim 4); at col., e.g., col. 20, lines 46-53, teach microarray plates reading upon a

solid support, wherein the microarray plates are information carriers which carry information in electronic and digitized form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a microarray plate that is a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and at col. 9, lines 23-55, teach electroflow media, reading on solvents, wherein said media includes polysaccharides, agarose, natural and synthetic polymers such as methylcellulose, polyacrylamide, hydrogels. Bjornson et al., at col. 18, lines 24-61, especially lines 56-59; col. 30, line 56-col. 31, line 14, disclose the manipulation of bead and particles in the channels of their disclosed microfluidic arrays. Bjornson et al. at col. 29, line 66-col. 30, line 14, teach using microfluidic processing for assay that determining specific binding pair members, as in determining an analyte, and including cell surface binding assays, assays for drug discovery and screening, and studies of receptors.

It would have been *prima facie* obvious at the time of the invention for one of ordinary skill in the art to have used methods comprising methods of screening of analytes, comprising applying a plurality of analytes onto solid supports, such that the analytes remain isolated from one another, and wherein the analytes are released after contact of the analyte-carrying solid supports; and wherein the analytes are disposed within individually identifiable containers, and transferring the analytes from the containers to the at least one solid support in such a manner as to maintain the transferred contents of each container separate from those of each other container, (as in claim 2); wherein the individually identifiable containers are an array of capillary tubes, (as in claim 3); wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the at least one solid support occurs by dispensing thereof through the open ends of the capillary tubes, (as in claim 4); wherein the solid support is an information carrier which carries information in electronic or digitised form, (as in claim 18); wherein each analyte-bearing solid support is contacted in step b) with a target provided from a separate compartment of a multi-compartmented apparatus, (as in claim 27); wherein said compartments are an arrangement of mini-wells in said apparatus, (as in claim 28); and wherein the analyte dissolves in a solvent, wherein said solvent includes polysaccharides, agarose, natural and synthetic polymers, methylcellulose, polyacrylamide, hydrogels, such that each analyte following application to the solid support and drying, liquefies in response to said chemical or physical parameter, (as in claim 31).

One of ordinary skill in the art would have been motivated to use methods of screening analytes, wherein the analytes are beads comprising oligomeric molecules, wherein the beads are applied to a substrate, as taught by Lerner (see, e.g., Lerner at col. 21, lines 33-43); and wherein the bead/analytes are manipulated in microarray plates that comprise compartments and capillary tubes, wherein the microarray plates are solid supports that are electronic, digital information carriers and further comprising media, as taught by Bjornson above, because Bjornson teaches manipulation of analytes or beads within microarray plates, and Bjornson teaches evaluating analyte binding to cell surfaces, for example, in order to identify specific binding pairs, and so to screen for potential drugs that target cell surface receptors.

One of ordinary skill in the art would have had a reasonable expectation of success in using bead analytes applied onto substrates, wherein those substrates are electronic microarrays comprising compartments, capillary tubes, and media, because, absent evidence to the contrary, beads or particles that release compounds into solution were known in the medicinal arts and because flowing particles through such arrays, absent evidence to the contrary, were known in the microfluidic arts.

Response to Arguments

Applicant states in the Reply at p. 5, the language of cancelled claims 2-4, 9 and 36 was incorporated into amended claim 1. Because former claims 1-4, 9 and 36, were rejected as unpatentable over the teachings of the prior art references of Lerner and Bjornson, the instant rejection is maintained.

Applicant, in the Reply, reviews the previous Office action, and at p. 15, requests further clarification of the teachings of Bjornson et al., in regard to gathering data via an electronic, magnetic or digitized means. Applicant, in the Reply at pp. 16-17, argues that a *prima facie* case of obviousness has not been established, at least because there is no suggestion or motivation to modify the references; and

applicant argues that the references when combined, do not teach or suggest all claim limitations of the currently pending, amended claims.

Applicant's arguments entered 9/14/2005 have been fully considered but they are not persuasive.

In regard to data collection, Bjornson at, e.g., col. 28, lines 37-42, teach assays and screening methods that employ detection means including, but not limited to spectrophotometric, chemiluminescent, electrochemical or radio chemical means. Bjornson at, e.g., col. 20, lines 46-65, teach the use of an electronic computer connected to electrodes, wherein the electrodes are made interactive with an optical detection device, such as an ultraviolet or fluorescent spectrometer. Therefore, examiner respectfully submits that Bjornson teaches gathering data by electronic, magnetic or digitized means.

Bjornson et al., disclose motivation to combine the reference, as applicant notes in the Reply at p. 14, para 2, the previous Office action states:

> One of ordinary skill in the art would have been motivated to use methods of screening analytes, wherein the analytes are beads comprising oligomeric molecules, wherein the beads are applied to a substrate, as taught by Lerner (see, e.g., Lerner at col. 21, lines 33-43); and wherein the bead/analytes are manipulated in microarray plates that comprise compartments and capillary tubes, wherein the microarray plates are solid supports that are electronic, digital information carriers and further comprising media, as taught by Bjornson above, because Bjornson teaches manipulation of analytes or beads within microarray plates, and Bjornson teaches evaluating analyte binding to cell surfaces, for example, in order to identify specific binding pairs, and so to screen for potential drugs that target cell surface receptors.

Office action, mailed 6/17/2005, at pp. 14-15, bridging paragraph. In particular, Bjornson at, e.g., col. 24, lines 27-43, disclose dispensing liquid drops through capillary size dispensing tubes onto substrates surfaces in miniature arrays, wherein the arrays may consist of nucleic acids, peptides, immunoassay reagents, pharmaceutical test compounds, and the like.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As shown above, the examiner respectfully submits that motivation to combine the references may be found at least within the prior art reference of Bjornson et al. The examiner respectfully submits that applicant's arguments do not *refute* the aforementioned reasons for motivation to combine the references, as set forth in the previous Office action. Therefore, the examiner respectfully urges that a *prima facie* case of obviousness has, indeed, been established.

Response to Arguments

Applicant argues that Bjornson et al. do not teach or suggest that analytes attached to and subsequently cleaved from beads as described in Lerner could be used in its devices and methods. Applicant argues that the practitioner would not look to Bjornson et al., for a device or methods for utilizing individual containers or capillaries to

bring a bead-analyte complex into proximity with a target. Therefore, there is no motivation to combine the teachings of the references. Applicant argues that there is no teaching or suggestion in Bjornson et al., to attach analytes to beads or otherwise utilize beads as a carrier to bring an analyte in proximity to a target for analysis, and there is no teaching or suggestion to screen analytes (beads or not) using the methods as claimed in the present invention.

Applicant's arguments, entered 4/26/2006, have been fully considered but they are not persuasive. Bjornson et al., in the background of the invention, at col. 2, lines 35-42, teach the coating of beads with an acceptor molecule in homogeneous assays. Bjornson et al., at col. 30, line 34-55, contemplate the use of heterogeneous and homogeneous assays, and at col. 30, line 56-col. 31, line 14, contemplate kits that comprise magnetic beads, non-magnetic particles and beads. Thus, the examiner respectfully submits that Bjornson et al. suggest that beads, (and as described in Lerner), could be used in its devices and methods, and that prima facie obviousness of the instant claimed invention is shown is demonstrated. It is respectfully noted that Bjornson et al., at col. 1, lines 8-18, teach the invention in the context of screening combinatorial libraries, where it would be desirable to use devices and automated methods for transferring many analytes, i.e., targets and ligands, or ligands and antiligands, or targets and antitargets.

Conclusion

9. Claims 1, 5, 10, 17, 18, 24, 26, 29, 30, and 32-35 stand finally rejected.

10. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark L. Shibuya
Examiner
Art Unit 1639